

## **Remarks**

Claims 1-58 are currently pending in the application. Claims 48-58 are withdrawn from consideration at this time. Claims 1-47 currently stand rejected. Claims 1, 2, 5, 8, 14, and 32-35 have been amended. All other pending claims remain unchanged. Applicant respectfully submits that no new matter is added through the amendment to the claims. Each of the rejections levied in the Office Action is address individually below.

The claims have been amended in response to the examiner's suggestions. The deletion of any claims and any other loss of claimed subject matter is being made solely to expedite prosecution of the subject matter now claimed. Applicant is submitting the present amendment without prejudice to the subsequent prosecution of claims on canceled subject matter. Applicant explicitly reserves the right to pursue the subject matter of any of the canceled or amended claims, in applications which claim priority to the present application.

### **1. Rejections under 35 U.S.C. § 112, second paragraph, for indefiniteness.**

Claims 5-8 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Specifically, claims 5 and 8 have been rejected for reciting 'wherein each occurrence of L1 is a natural amino acid side chain,' which the Examiner regards as not definite. The claims have been amended to obviate this rejection, and Applicant respectfully submits that amended claims 5 and 8 are definite.

### **2. Rejections under 35 U.S.C. § 112, first paragraph, for lack of enablement.**

Claims 1-3, 5-19, 21-30, and 32-47 are rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement.

In particular, the Examiner regards the scope of the instant claims as comprising a greater degree of variance with respect to the carbohydrate moieties and that the means to

make such moieties and the means to use said moieties are unknown. The Examiner states that one of skill in the art would be subject to undue experimentation in order to make and use all the structures within the scope of the claims. Applicant disagrees.

In order to be enabling, the Applicant is not required to teach the synthesis of all possible carbohydrate moieties. Only a representative number of examples as described in the application need to be shown to enable the claims. The generality of the preparation of glycoamino acids and the inventive glycopeptides is addressed throughout the specification, particularly pp. 113-117 and p. 164, paragraph 0398. The synthetic methods disclosed in the present application apply to a broad substrate base, and therefore no undue experimentation is necessary to prepare the claimed compounds.

The Examiner admits the specification teaches how to make glycopeptides comprising Globo-H, fucosyl GM1, KH-1, glycophorin, STN, Ley, N3, Tn, 2,6 Tn, 2,3 ST, and TF, but the Examiner cites Sierra and de la Torre (*Angewandte Chemie*, 2000, Vol. 39, pp. 1538-1559) to suggest that the synthesis of other multiantigenic glycopeptides of the instant claims would be impossible without undue experimentation. Applicant disagrees. Of all of the chemical syntheses reviewed by Sierra and de la Torre, not one involves the synthesis of a glycopeptide, peptide, or polysaccharide. Moreover, none of the chemical transformations referred to in the article deal with carbohydrate moieties or peptides. The structural complexities and synthetic approaches towards the molecules reviewed by Sierra and de la Torre are categorically different from the glycopeptide constructs taught by the present invention. One skilled in the art will appreciate that the fields of carbohydrate and peptide synthesis are relatively mature, and there are a plethora of well-understood, general synthetic methodologies available to synthesize complex carbohydrates and peptides, disclosed herein and elsewhere (for a review on carbohydrate chemistry, see *Angewandte Chemie Int. Ed.*, 2001, Vol. 40, pp. 1576-1624).

While the examiner admits that the specification teaches the synthesis and use of pyranose moieties, the Examiner does not believe the specification supports the synthesis and use of furanose. Applicant disagrees. The synthetic methods in the specification could be adapted by one of ordinary skill in the art to prepare pyranose as well as furanose moieties. The glycopeptides containing furanose moieties could then be used in

immunogenic pharmaceutical compositions as described in the specification. Although Applicant believes both furanose and pyranose moieties are fully supported, Applicant has chosen to amend the claims to recite only pyranose rings in order to further prosecution. Applicant reserves the right to pursue claims reciting furanose moieties in future applications claiming priority to the present case. Applicant respectfully submits that the Examiner's rejection is rendered moot by the present amendment.

Furthermore, the Examiner maintains that the specification provides no teachings as to how to use a glycopeptide construct that is not a known antigenic domain which would evoke an efficacious immune response in a patient. Applicant disagrees. A claim is not invalid merely because it includes some inoperative embodiments (i.e., carbohydrate domains that would not successfully vaccinate a subject against a tumor). *Atlas Powder Co. v. E. I. du Pont de Nemours & Co.*, 750 F.2d 1569, 224 USPQ 409 (Fed. Cir. 1984) ("It is not a function of the claims to specifically exclude . . . possible inoperative substances . . . ." *In re Dinh-Nguyen*, 492 F.2d 856, 858-59, 181 USPQ 46, 48 (CCPA 1974)). While Applicant believes the claims are fully enabled, in order to expedite prosecution, Applicant has chosen to amend the claims to limit each occurrence of A to a carbohydrate domain that has been found to be present on tumor cells. Applicant respectfully submits that the Examiner's rejection is rendered moot by the present amendment.

Applicant respectfully submits that the claims as amended are fully enabled and requests that the rejection be removed.

**3. Rejections under 35 U.S.C. § 102(b), for anticipation.** Claims 1, 2, 4-6, 9-13, 21-28, and 47 are rejected under 35 U.S.C. § 102(b), as being anticipated by Danishefsky et al. (WO98/46246). The Examiner cites WO98/46246 for disclosing a composition comprising a clustered O-linked glycopeptidic moiety wherein the glycopeptide incorporates glycosyl units with clustered ST epitopes in addition to glycopeptides wherein the carbohydrate domains are MBr1 (Globo-H), truncated MBr1 epitope (pentasaccharide), truncated MBr1 epitope (tetrasaccharide), SSEA-3 antigen, Le<sup>y</sup> and GM1. WO98/46246 discloses clustered O-linked glycopeptide constructs in which *only*

*one cluster* of carbohydrate antigen is attached to a peptide backbone (i.e., up to three antigens on adjacent amino acids) and/or immunogenic carrier molecule. However, WO98/46246 does not teach the strategy of the present invention, wherein *multiple clusters* of different carbohydrate antigens are displayed on a single polypeptide backbone (i.e., one cluster of one antigen linked to one cluster of a different antigen). This “clusters of clusters” approach may be a more accurate mimic of the display of carbohydrates on the surface of transformed cells. It is postulated that this strategy will induce a more robust immune response toward transformed cells expressing more than one antigen, and is elaborated in the specification, pp. 140-143.

The Examiner further maintains that WO98/46246 discloses constructs comprising linkers, definitions of  $R^{X1}$ , crosslinkers, immunogenic or lipopeptide carriers, attachment of said carriers to a glycopeptide, and methods of making structures and conjugates which fulfill the embodiments of the rejected claims. However, in each case these Danishefsky et al. disclosures comprise glycopeptide constructs in which *only one cluster* of carbohydrate antigen is attached to a peptide backbone, and therefore do not anticipate the presently claimed constructs comprising *multiple clusters* of different carbohydrate antigens displayed on a single polypeptide backbone. Applicant respectfully requests that the rejection be removed.

**4. Double Patenting.** The Examiner has provisionally rejected claims 1, 3-6, 9-35, and 37-47 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 56, 58-62, 65-67, 69-76, 78-81, 84-86, and 88-98 of co-pending Application No. 09/641,742, and the Examiner has provisionally rejected claims 1, 3-7, 9-22, 24, 31-33, 35, 37, 39, 40, and 43-47 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 118-129, 132-137, 138-146, and 148-168 of copending Application No. 10/209,618. At this time, Applicant respectfully refrains from commenting on these double patenting issues until the provisional rejections mature into actual rejections.

In view of the foregoing amendments and arguments, Applicant respectfully submits that the present case is now in condition for allowance. A Notice to that effect is requested.

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Respectfully submitted,

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Date: January 18, 2008